REMARKS

With the entry of this Amendment, claims 23-36 are now pending in the application. Applicants file this supplementary amendment to correct the previously filed Amendment, dated March 9, 2004. That amendment inadvertently did not list claims 1-22 as cancelled in the listing of the claims.

Support for new claims 31-39 may be found in the original claims, as well as in the specification in Figure 3E-F; page 12, lines 11-18; page 16, lines 15-20; page 23, lines 30-35.

Written Description Rejection

The Examiner has rejected claims 23-30 as allegedly lacking written description under 35 U.S.C. § 112, first paragraph. The Examiner believes that the original application does not provide adequate support for the broadly claimed genus of immunogenic polypeptide fragments comprising HIV-1_{MAL} epitopes of 5-150 amino acid residues, wherein at least one amino acid residue is substituted in all of the sequences designated HIV-1_{BRU}, HIV-1_{ARV-2}, or HIV-1_{ELI}. Specifically, the Examiner asserts that the claim limitations are functional limitations and that the specification does not teach which amino acids are necessary for immunogenicity. Furthermore, the Examiner asserts that the 5-150 limitation is not supported as that numerical limitation is actually used to describe "hybrid polypeptides" or fusion proteins, not immunogenic polypeptide fragments.

SUPPORT FOR MUTATIONS

The Examiner seems primarily concerned with the substitutions in the LAV_{MAL} sequences. In particular, the Examiner is concerned that the claims recite mutations of the LAV_{MAL} sequence without specifying how many amino acids are mutated or which amino acids are mutated. The Examiner argues that the claims and specification fail to provide any information on which sequences can be mutated without eliminating immunogenicity.

Applicants believe that comparison of the various Env sequences in Figure 3 shows that positions where the amino acid is substituted in all of the sequences designated LAV_{BRU}, ARV2, and LAV_{ELI} when compared to LAV_{MAL} shows that this particular amino acid is not required for immunogenicity. This information assists one in understanding which Env sequences were not required for immunogenicity and shows that this was understood by the inventors at the earliest filing date.

Nevertheless, Applicants have amended the claims to recite amino acids that may be substituted in an effort to facilitate prosecution. Specifically, the claims recite that the LAV_{MAL} fragments have at least one substitution at one or more of positions 8, 9, 90, 102, 131, 133, 140, 156, 172, 177, 179, 185, 188, 192, 198, 207, 209, 290, 305, 308, 323, 333, 335, 337, 341, 342, 353, 356, 359, 363, 404, 428, 440, 457, 41, 477, 483, 484, 486, 538, 555, 641, 652, 656, 660, 663, 694, 740, 733, 799, 854, 856, 862, and 875 of Env as shown in Figures 3E-F. This amendment does not require all of these substitutions.

These mutant LAV_{MAL} fragments were within the original invention and believed to be immunogenic as the listed positions are not conserved among the four LAV virus sequences provided in this application.

Additionally, the specification provides affirmative information on which sequences are beneficial for immunogenicity. Applicants have added dependent claims reciting that the fragments contain at least one well-conserved sequence. The specification identifies well-conserved stretches at positions 37-130, 211-289, and 488-530 of Env in Fig. 3E. *See* Specification page 12, lines 11-18. The specification also refers to conserved sequences between positions 490-620 of Env in Fig. 3E. *See* Specification page 16, lines 15-20. The specification further states that proteins containing or consisting of these "well conserved stretches" are of particular interest for the production of immunogenic compositions. *See* Specification, page 23, lines 30-35. This section also mentions positions 531-877 and 680-700. Thus, this shows that Applicants understood which sequences were beneficial for immunogenicity.

FRAGMENT LENGTH

Turning to the question of fragment length, the specification refers to hybrid polypeptides on page 28, as the Examiner indicated. However, on page 34 it also describes vaccine compositions comprising "peptides containing less than 250 amino acid units, preferably less than 150, particularly from 1 to 150 amino acid residues, as deducible for the complete genome of LAV_{MAL}." Thus, the specification does support fragments of LAV_{MAL} with the specified length, not just hybrid polypeptides as described on page 28.

Additionally, the specification does provide information on particular immunogenic fragments on page 23, as the specification indicates that proteins could be "comprising or consisting of the 'well conserved stretches.'" This means that the fragments could have the number of amino acids in that stretch (i.e., consisting of) or a greater number (comprising). As these stretches contain 530, 497, 347, 21, 94, 79, 43, and 131 amino acids, respectively, Applicants believe that there is support for fragments of 21-131 amino acids in length, as well as fragments of 21, 43, 79, 97, and 131 amino acids in length. Applicants have added claims reciting these limitations.

Therefore, Applicants believe the invention is supported by the written description in the specification and that this rejection should be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

If there is any fee due in connection with the filing of this Supplemental Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: April 7, 2004

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